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Short communication

Impulse control disorder and rapid eye movement sleep behavior disorder in Parkinson's disease

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ABSTRACT

Introduction: The relationship between ICD and RBD is still not yet understood and the results from the current literature are contradictory in PD. We aimed to explore the association between rapid eye movement (REM) sleep behavior disorder (RBD) and impulse control disorder in Parkinson's disease.
Methods: Ninety-eight non-demented patients with Parkinson's disease underwent one night of video-polysomnography recording. The diagnosis of RBD was established according to clinical and polysomnographic criteria. Impulse control disorders were determined by a gold standard, semi-structured diagnostic interview.
Results: Half of the patients ($n = 49$) reported clinical history of RBD while polysomnographic diagnosis of RBD was confirmed in 31.6% of the patients ($n = 31$). At least one impulse control disorder was identified in 21.4% of patients, 22.6% with RBD and 20.9% without. Logistic regression controlling for potential confounders indicated that both clinical RBD (OR = 0.34, 95% CI = 0.07–1.48, $P = 0.15$) and polysomnographic confirmed RBD diagnoses (OR = 0.1.28, 95% CI = 0.31–5.33, $P = 0.34$) were not associated with impulse control disorder.
Conclusion: In Parkinson's disease, REM Sleep Behavior Disorder is not associated with impulse control disorder. The results of our study do not support the notion that PSG-confirmed RBD and ICD share a common pathophysiology.

1. Introduction

REM Sleep Behavior Disorder (RBD) and impulse control disorder (ICD) are two frequent disabling manifestations associated with Parkinson's disease (PD) [1,2]. The abnormal behaviors that characterize ICD are based on reward-processing dysfunctions and reward-processing abnormalities which have recently been described in patients with idiopathic RBD [3,4]. The relationship between ICD and RBD is still not yet understood and the results from the current literature are contradictory in PD [5–7]. Our objective was to clarify the potential relationship between polysomnography-confirmed RBD and ICD based on a semi-structured diagnostic interview in non-demented patients with idiopathic PD.

2. Patients and methods

2.1. Patients

From January 2008 to June 2012, 98 non-demented patients with idiopathic PD (males: 64; median age: 66.5, range: 45–86) were enrolled in this study. Patients who had been diagnosed with idiopathic PD according to the Queen Square Brain Bank criteria and gave informed consent met inclusion criteria. Dementia was excluded using specific diagnostic clinical criteria [8]. Demographic data, disease

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characteristics and medication (with particular attention to dopamine agonists and psychoactive drugs) were collected during a face-to-face interview. Severity of motor symptoms was measured by the Unified Parkinson's Disease Rating Scale (UPDRS, Section III) and the Hoehn and Yahr scale in the "on" state. The levodopa equivalent daily dose (LEDD) was calculated both for dopamine agonists (DA-LEDD) and for the dopamine agonists + L-dopa (total LEDD).

2.2. Diagnosis of RBD

RBD was diagnosed by a neurologist according to the *International Classification of Sleep Disorders, second edition* (ICSDII) criteria and along international recommendations that is, the presence of excessive muscle activity during rapid-eye-movement (REM) sleep (>30% of REM sleep with tonic EMG activity or >15% of REM sleep with phasic EMG activity) and ≥1 of the following: history of dream-enactment behaviors or abnormal REM sleep behaviors confirmed by polysomnographic (PSG) monitoring with synchronized videotape [9,10].

2.3. Diagnosis of ICD

All patients were administered a "gold standard", semi-structured diagnostic interview for current pathological gambling, compulsive buying, hypersexuality, compulsive eating, compulsive medication use, punding by experienced psychologist (AR, MCL and SB) [2].

3. Procedure

Consecutive PD patients seen in clinic at the University Hospital Gui-de-Chauliac (Montpellier, France) were asked to participate in this study which required an overnight PSG, 98 agreed. At time of study, all patients with PD were examined by movement disorder specialists (BC, CG, MC and VCDC). All PSG were scored by a fully trained neurologist blinded to clinical patient's status (HY). All patients gave informed consent according to the Declaration of Helsinki. Ethics approval was obtained from the hospital's ethics committee. Participants did not receive any financial compensation for their participation.

3.1. Statistical analysis

Statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS) version 19 for windows (Chicago, SPSS Inc.). Data were examined for normal distribution (tested with Kolmogorov–Smirnov test). As all continuous variables were not normally distributed, median [minimum–maximum] were used. Data were expressed as percentage for the categorical variables. Odds ratios (OR) and their confidence intervals (CI) were estimated using a conditional logistic regression model. The level of significance was set at $P < 0.05$.

4. Results

4.1. Clinical characteristics

The PD duration at the time of study was 8 years [1–23]. The motor severity of the disease was 2 [1–3] scored on the Hoehn and Yahr scale and 26 [5–80] on the UPDRS-III scale. Antiparkinsonian drugs with at least one DA was reported in 73.5% (DA-LEDD = 300 [24–1000]) and L-dopa in 89.8% (LEDD = 600 [150–1500]) of patients. The total LEDD was 833 mg [317–2033]. Twenty-five patients (25.5.7%) were taking antidepressants and 22 (22.4%) benzodiazepines.

4.2. RBD characteristics

Half of the patients ($n = 49$) reported clinical history of dream-enactment or witnessed dream enactment. Onset of RBD symptoms data was available for 31 patients (/49). Five patients had no bed partner and the others ($n = 13$) were not able to date their symptoms onset. Twenty patients indicated that their RBD symptoms appeared after PD onset and four reported a co-occurrence between RBD and PD symptoms. Seven patients reported that their RBD symptoms predated PD onset.

PSG-confirmed RBD was found in 31.6% of the patients ($n = 31$). On the whole sample, 21 patients (21.4%) had a tonic EMG density score >30% (median = 5.71 [0–88]) and 23 (23.5%) a phasic chin EMG score > 15% (median = 8.79 [0–66]). Ten patients (10.2%) scored above both tonic and phasic cut-offs. Clinical history of RBD was systematically reported in patients who scored above tonic EMG muscle activity cut-off (>30%). Excepted for three patients, same pattern was observed for phasic EMG density cut-off (>15%).

4.3. ICD characteristics

At least one active ICD was identified in 21.4% of patients ($n = 21$). Frequencies of active ICDs were as follows: compulsive sexual behavior (7.1%), pathological gambling (2%), compulsive buying (4.1%), binge-eating disorder (2%), and punding (14.3%). Approximately 8% of patients had comorbid ICDs.

4.4. Association between ICD and RBD

Logistic regression model controlling for potential confounders (i.e., age, gender, disease severity and duration, LEDD and depression) indicated that RBD based solely on clinical criteria was not associated to ICD (OR = 0.34, 95% CI = 0.07–1.48, $P = 0.15$). ICD was found in 20.4% ($n = 10/49$) of patients with clinical history of RBD and in 22.4% ($n = 11/49$) of patients without RBD (Fig. 1A). Similarly, polysomnographic confirmed RBD diagnosis was unrelated to ICD (OR = 0.1.28, 95% CI = 0.31–5.33, $P = 0.34$). ICD was found in 22.6% ($n = 7/31$) of patients with RBD based on international criteria and in 20.87% ($n = 14/67$) of patients without RBD (Fig. 1B). Tonic and tonic chin EMG scores were not related to ICD (respectively, $P = 0.36$ and $P = 0.88$; Fig. 2). Same pattern of results was observed when considering the cut-off scores. Finally, we performed subgroup analyses on patients with total LEDD >1000 mg. In this group ($n = 23$), 7 patients had a PSG-confirmed RBD (30.4%) and 12 had clinical history of dream-enactment (52.2%). These two proportions are very similar to those observed on the whole sample (31.6% and 50%).

5. Discussion

In the present study, RBD based on international criteria and ICD were detected in respectively 30.6% and 21.4% of the patients. These values are in the range of those reported in literature [1,2]. We confirmed RBD according the recommended international criteria with a PSG that rules out mimics such as severe obstructive sleep apnea and non-REM parasomnia. ICD were diagnosed through a standardized face-to-face clinical interview. Using these robust diagnostic criteria, we failed to find any association between both clinical and PSG-confirmed RBD and ICD. Furthermore, there were no significant differences between patients with and without ICD in both phasic and tonic EMG density scores. These negative results are in accordance with those reported by Romenets and coworkers who found no association between ICD (i.e. compulsive gambling, hypersexuality, excessive spending and punding) and PSG-confirmed RBD in PD [7].

Considering the clinical definition of RBD, a questionnaire-based study using the RBD Screening Questionnaire and the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease's (QUIP) reported that probable RBD increased frequency of ICD symptoms in PD [5]. The QUIP is undoubtedly a very useful screening instrument for ICD. However, this tool has low predictive positive value implying the need of clinical interview to verify if the

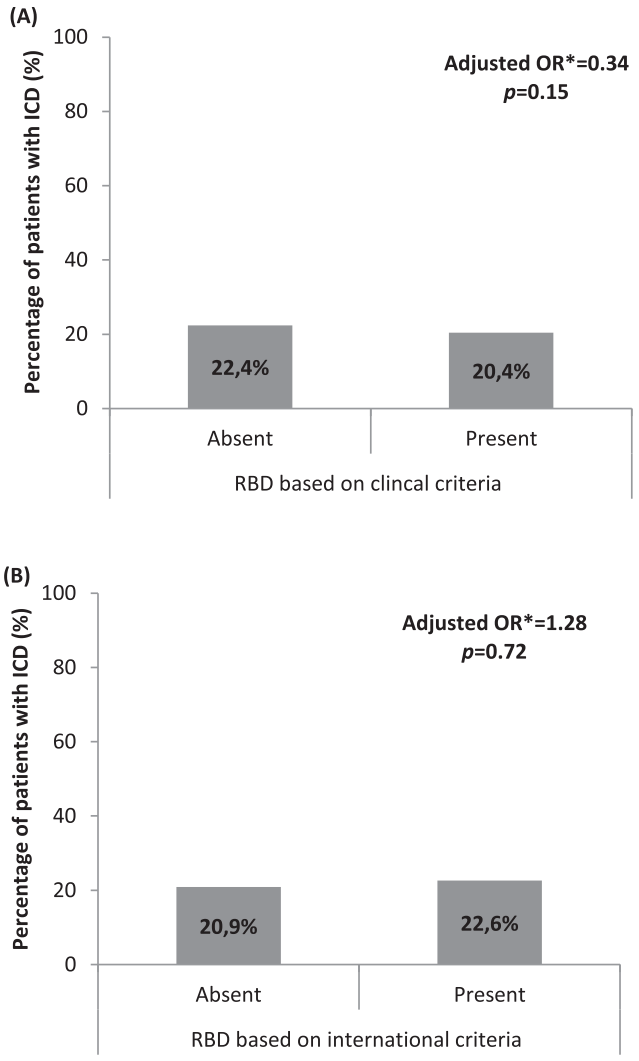

Fig. 1. Percentage of patients with and without impulse control disorder (ICD) depending on the presence or absent of idiopathic rapid eye movement sleep behavior disorder (RBD) based on clinical criteria (A) and on international criteria (B).

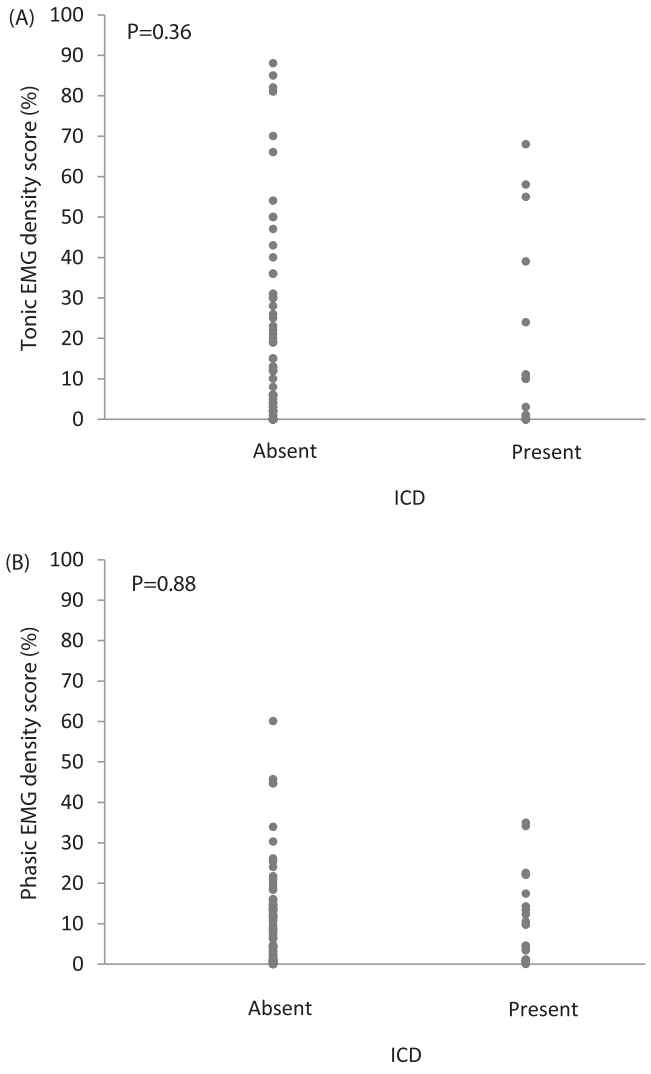

Fig. 2. Individual values of phasic (A) and tonic (B) EMG density scores (%) depending on the presence or absent of impulse control disorder (ICD).

patient truly has clinically significant ICD. In that respect, one or more ICD were found in 48% of the patients ($n = 106/220$) in that study. This value largely exceeds those classically reported. In agreement with our results, a very recent cross sectional study including 944 patients with PD, failed to corroborate the relationship between clinically probable RBD (ICSDII) and ICD assessed by the Minnesota Impulsive Disorders Interview [6].

Data from the literature show an undeniable association between impulse control disorders and LEDD in PD [2]. However, the relationship between the latter and polysomnographic confirmed RBD diagnosis is still under debate. Only one polysomnographic study performed on a large cohort ($n = 351$) reported that RBD in PD was determined by higher dose of levodopa ($P < 0.001$) [11]. Some other studies, ours included, did not support this association [7,12,13]. Interestingly, a very recent study from the German group showed the presence of REM sleep behavioral events (i.e. motor behaviors and/or vocalizations in REM sleep with a purposeful component other than comfort moves) in 81 of 158 newly diagnosed, unmedicated patients with PD [14]. These results suggested that polysomnographic RBD features are observed in the absence of dopaminergic medication. Finally, contrary to ICD, reduction of dopaminergic agents does not systematically relieve RBD manifestations and efficacy studies have shown contradictory results [15].

The clinical manifestations of the ICDs are heterogeneous and the pathophysiology of these behavioral disruptions is still not clear [2]. In the future, it would be interesting to consider homogeneous ICD entities when studying their association with PSG-confirmed RBD. Furthermore, longitudinal studies including larger cohorts of subjects are needed to examine the evolution of changes in muscle activity during REM sleep and its possible relevance as a predictor of ICD in PD.

To conclude, the results of our study do not support the notion that PSG-confirmed RBD and ICD share a common pathophysiology.

Author contributions

1. Research project: A. Conception, B. Organization, C. Execution. 2. Analysis: A. Design, B. Execution, C. Review and Critique. 3. Manuscript: A. Writing of the first draft, B. Review and Critique. Sophie Bayard: 1A, 1B, 1C, 2A, 2B, 2C, 3A. Yves Dauvilliers: 1A, 2A, 2C, 3B. Muriel Croisier Langenier: 1B, 1C, 3B. Mahmoud Charif: 1C, 3B. Christian Geny: 1C, 3B. Bertrand Carlander: 1C, 3B. Huan Hu: 1C, 2B, 3B. Valérie Cochen De Cock: 1C, 2A, 2B, 2C, 3A, 3B.

Disclosure statements

Professor Dauvilliers has received speaker's honoraria and funding for travel to conferences from UCB Pharma, Cephalon, Novartis, Jazz, and Bioprojet. Prof. Dauvilliers has participated in advisory boards of UCB and Bioprojet. Dr Cochen De Cock has speaker's honoraria and fundings for travel to conferences from UCB Pharma, TEVA/Lundbeck, Bastide and SOS oxygene. Ms. Bayard, Croisier Langenier, Drs Carlander, Charif, Geny, and Huan Yu report no financial conflicts of interest.

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